

Theoretical Issues Pertinent to Measurement of Quality of Life

Meriel E.M. Jenney, MD, MRCP*

INTRODUCTION

We are in the privileged position in paediatric oncology, to now be concerned with the long term outcome that results from curing childhood cancer. With the improved survival rates however has come an increasing understanding of significant, often adverse late effects of therapy. What is not yet known is the impact that such late effects have on the quality of life (QoL) of the survivor. Interest in the measurement of QoL has dramatically expanded over the past 5 years, with an increasing appreciation of the importance of the patient's perspective. However the inadequacy of reporting data relating to QoL within the medical literature has been highlighted recently [1]. In particular, there is a lack of clarification relating to what is being measured, why it is being measured, and whether there has been any good evidence presented that the measure is valid. This review will attempt to clarify these points and will also address the more complex issue of how measurement of QoL in children and adolescents and in adults, particularly within the context of survivors of childhood cancer, can be approached.

WHAT IS QoL?

QoL is difficult to define. Its meaning depends, at least in part, on the context in which it is used—Emphasis may be placed on social, environmental, or political issues rather than the health of the individual. For example, the QoL of refugees would be affected most greatly by social, environmental, and political issues, whereas physical and emotional functioning may affect the QoL of a child with a terminal disease, a student, or a young mother. Within the context of health and medical outcome assessments, the impact of health on the QoL of the individual, in most circumstances, is what the observer wishes to measure. Accordingly, the term “health-related QoL” (HRQL) has been introduced. It is useful, in that it emphasises the impact of health on the much broader concept of QoL but also acknowledges that issues beyond physical functioning are assessed. An important aspect of the definition of QoL is the personal perspective; essentially, one is attempting to assess the uniquely subjective perception of how individual patients feel about their health status and/ or nonmedical aspects of their lives [2]. From a psychometric point of view,

QoL is a multidimensional construct that encompasses physical, mental, social, emotional, and behavioral components of well being and functioning [3].

Consideration of HRQL in children and adolescents is still more complex. Child health has been defined as “the ability to participate fully in developmentally appropriate activities and requires physical, psychological, and social energy” [4]. It is normal for a child to change; as a child matures, not only do his or her physical and mental abilities increase, but the child's understanding of health and well being also changes [5,6]. Furthermore, the issues of importance when considering HRQL, for example, at the age of 8 years (e.g., physical ability, family relationships), may be very different from the issues that are important to an adolescent for whom body image, self esteem, and peer relationships may be of considerably greater concern.

WHY MEASURE QoL?

For children with cancer, survival remains the principal aim of therapy. However, because survival rates have improved dramatically over the past 30 years, and late effects of therapy have been recognised, there has been an appreciation that the impact of such sequelae, as perceived by the patient, is not known. Furthermore, the majority of survivors of childhood cancer would be expected to have a near-normal life expectancy. Without measures of QoL, assumptions are made with respect to the relative importance of different late effects of therapy for childhood cancer. Is it better to be infertile or to have impairment of cardiac function following therapy for Hodgkins disease? Only the patient can give us the answer. Unless the issues of importance to the survivors of childhood cancer are understood, future studies will not be designed to minimise such late effects, and it will not be possible to provide support to minimise adverse effects on QoL or to assess the success of any such intervention.

There has been an increasing recognition of the need to incorporate assessment of QoL into clinical trials. A joint working group of the Food and Drug Administra-

The Royal Manchester Children's Hospital, Pendlebury, Manchester, United Kingdom

*Correspondence to: Meriel E.M. Jenney, Llandough Hospital, NHS Trust, Penlan Road, Penarth CF64 2XX, U.K.

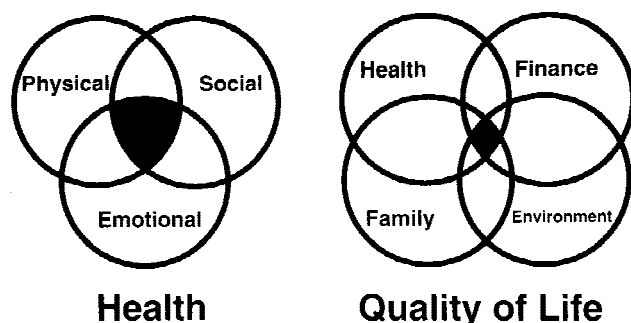


Fig. 1. The concept of health-related quality of life.

tion and the National Cancer Institute recommended that end points in clinical trials should include an assessment of QoL [7]. If this is to be done, then it is vital that the instruments used are practical, acceptable, reliable, and valid.

In addition to their role within clinical trials, there is a need to identify, on an individual basis, issues that may adversely affect a patient's QoL. Ideally, an instrument could be used effectively in both situations and allow reassessment of any intervention designed to improve QoL.

One other reason for attempting to understand and measure QoL is to provide for the increasing demand for informed choice for patients and their parents. As survival rates continue to improve, issues relating to QoL assume more importance and the priorities of recipients of health care should be recognised.

HOW CAN ONE MEASURE HRQL?

Conceptually, one must return to the definition of health and QoL to determine how it can be measured. For the majority of investigators, it is the impact of health on QoL (or HRQL) that is to be assessed (see Fig. 1).

Domains

The conceptual arguments relating to the use of categories or domains to measure QoL have been established previously in adults through the RAND Health Insurance Experiment and are used extensively in measures for adults, (e.g., SF36 and Nottingham Health Profile [8,9]. Essentially, health is described as a series of discrete yet overlapping areas known as dimensions or domains. Examples of the domains of health identified to be important to survivors of childhood cancer in a pilot study are presented in Table I. The standard approach to measurement of "functioning" in each domain is that a series of questions are developed, which probe that particular area of health. Statistical reliability can be demonstrated by using analyses such as Cronbach's alpha [10] or factor analysis [11] to demonstrate that the questions within a domain correlate with one another and

TABLE I. Domains of Health Identified by Survivors of Childhood Cancer

Physical activity	Peer relationships
Physical energy	Pain
Emotion	School
Physical appearance	Outlook
Family	

differ between domains. However, the distinction between domains is not necessarily complete—For example, a high level of pain or discomfort could clearly lead to impairment of functioning within the dimension of physical activity.

Generic Versus Disease-Specific Measures

There are two basic approaches to measurement of health-related QoL: Each has advantages and disadvantages. The use of a disease-specific measure allows detailed assessment of symptoms and concerns that are pertinent to a particular group of patients without the measure becoming too cumbersome. The principle aim of this approach is to increase the responsiveness of the measure by including only important aspects of HRQL that are relevant to the patients being studied. Such measures do not allow easy comparison between groups of patients.

Conversely, generic measures (measures designed for use with any illness group) allow comparisons between groups and (perhaps more importantly for children and adolescents) with peers. Although generic measures may lack sensitivity for some aspects of functioning for individual groups of patients, they provide the only objective means for comparisons between groups, allowing assessment of the impact of the disease and its treatment. The disadvantage of such measures is that they may not focus adequately on particular areas of concern for different groups of patients.

Mode of Administration

Measures of QoL are almost always in the format of a standardised questionnaire. This can be self administered, administered by face-to-face interview, or administered by telephone. Each has advantages and disadvantages [12]. For younger children, interviewing is required. Although this is expensive and relatively time consuming, one can expect a good response rate, and misunderstandings are generally avoided. The questionnaires are more likely to be fully completed. However, if possible, interviewers who are known to the subjects should be avoided to minimise bias. Self completion can be used for older children and adults (e.g., over 12 years of age). Although there may be lower response rates and a greater likelihood of misinterpretation of the items, subjects may be less inhibited and more honest in their response (less anxious to please). Telephone interviews

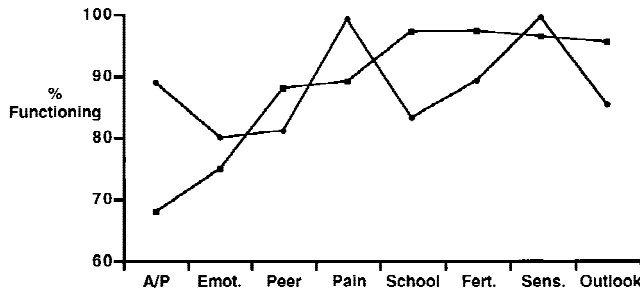


Fig. 2. Theoretical health profiles (not based on actual data) of survivors of childhood cancer. The graph shows possible perceived levels of functioning in a series of dimensions of health. A/P, activity; Emot, emotional functioning; Peer, peer relationships; Pain, pain discomfort; School, cognitive/school/work achievement; Sens, sensation (e.g., hearing/speech/sight); Outlook, overall outlook on life. Circles = survivors of leukemia; squares = survivors of bone tumors.

can be very effective, in that they are less expensive and can optimise completion and comprehension of the questionnaire.

It may not be possible to administer instruments to the patients themselves for a number of reasons, e.g., the patient is too sick or too young to respond or has inadequate comprehension. In this situation, proxy respondents can be used. The proxy may be the patient's care giver, parent, sibling, friend, or physician. The use of proxies has been shown to have limitations with clear differences in reporting of functional status between doctors and patients [13] and children and their care givers [14]. In certain circumstances, particularly those in which QoL may be considered to be poor by observers, the patient may deny any impairment. The use of proxy ratings may be of value in attempting to evaluate QoL in such situations and improve outcome wherever possible [15].

Presentation of Results

Within the context of generic instruments, there are two theoretical approaches to measurement and presentation of the scores obtained: health profiles and summary scores. The former allows more detailed assessments within domains and is therefore more responsive to change [16]. Subscale or domain scores can be provided that allow identification of specific areas of functioning that may be impaired. They may be essential for assessment of interventions that are designed to improve specific aspects of HRQL. A theoretical health profile for survivors of childhood cancer is shown in Figure 2.

A single summary score, or health index, may also be used that reflects overall HRQL. All of the items in the instrument are summed to provide an overall score (for example, in the multiattribute health status assessment and the Quality of Well-Being Scale) [17,18]. Such scores are useful for population comparisons and in cost-

benefit analyses. However, they do not provide details of specific areas of impairment of HRQL.

Utility measures provide a single summary score of HRQL but also take into account the preferences of individuals of different health states. They reflect both the health status of the individual and the value that the individual puts upon that health state.

Theoretical Issues Concerning Measurement of QoL in Children

In the context of paediatric oncology, consideration of measurement of QoL of adults is not sufficient. The QoL of the children both during therapy and after completion is important. This review has been concerned mostly with the use of standardised questionnaires for the assessment of QoL. If these are to be used with children, then one must be confident that the child's reading age and cognitive ability are adequate and that the child's interpretation of the questions and understanding of the issues addressed are appropriate. The reading age of the questionnaire can be assessed by using standards, such as the Flesch formula [19]. Questionnaires should be developed for use with different age groups, and consideration of the physical, emotional, and social development of the child should be made, with age-appropriate issues addressed. Determining the preferences or relative importance of particular issues at different ages may be of value. The importance of continued monitoring of QoL and development of age-appropriate scores may also be possible [20].

Measurement of QoL in the younger child remains a challenge. Although proxy ratings can be obtained, providing accurate assessments of the child's perspective is difficult. Further research exploring, for example, the use of pictures, videotapes, computers, qualitative data, and play is urgently required.

Validity and Reliability of Measures of QoL

It is essential that the instrument chosen for evaluation of QoL is valid for the population in which it is to be used. Reliability must also be demonstrated. In the absence of a gold standard of measurement of QoL for children and adolescents against which new measures can be assessed, it is important that new instruments demonstrate adequate validity and reliability using other criteria. This can be done in a number of ways, which are described briefly below.

Validity. Validity is the extent to which an instrument measures the desired underlying concept. A series of assessments can be made to demonstrate different aspects of the validity of the instrument [21].

Face validity describes the need for the questionnaire to apparently tap, simply by item (question) content, an underlying dimension. Questions should be unambiguous and easily understood and should reflect issues that are

appropriate to the dimension. *Content validity* is the extent to which items in a questionnaire tap all of the relevant aspects of the attribute they are attempting to measure.

Criterion validity is the extent to which a measure correlates with a preexisting one, preferably a “gold standard.” Although no overall gold standard exists for measurement of QoL, certain dimensions can be assessed by using gold standards that are accepted for that particular domain, e.g., comparison of the “emotion” domain with an established measure of mood or depression. There are two types of criterion validity: concurrent, in which a new measure is administered at the same time as a preexisting one, and the two are correlated, and predictive, in which the predictive power of the instrument can be compared against some other measure.

Construct validity is an assessment of the ability of an instrument to reflect prior hypotheses. For example, a lower QoL would be expected for children and adolescents who had required extensive surgery and radiotherapy (e.g., for pelvic soft tissue sarcomas) that resulted in multiple adverse effects (e.g., infertility, urinary diversion, colostomy). One would expect the measure to identify areas of impairment of HRQL. To establish convergent and discriminant validity, the results of the measure should correlate with results from other indicators that measure the same concept (convergent) and should not correlate with results from unrelated measures (discriminant).

Reliability. A reliable measure is one that produces consistent results from the same subject when there is no evidence of real change within that subject [21]. To establish *test-retest reliability*, the instrument is administered on two separate occasions to the same group of individuals. The two occasions should be far enough apart so that the previous responses cannot be remembered and close enough to minimise the chance of real change. The correlation between the two scores is an estimate of the measure’s reliability.

Interrater reliability is an assessment of the consistency of an instrument when it is administered by different interviewers. The time between interviews is short to minimise the chance of real change.

Internal consistency is the extent to which the items that are believed to be assessing the same dimension are actually doing so. Cronbach’s alpha is a statistical assessment of the correlation of items within a dimension [10].

Ceiling and floor effects. If an instrument is not sensitive to lower levels of illness or functioning, then it can be said to have floor effects, i.e., the respondents may score 0 on a scale 0–100 but may be capable of a further deterioration of health or functioning. Conversely, the measure may be insensitive to a relatively small impairment of HRQL: The majority of respondents would then

report high levels of functioning, and the measure would demonstrate a ceiling effect. Floor and ceiling effects are an indicator of the responsiveness of the instrument and are most likely to be found in instruments with small numbers of items (i.e., less responsive).

Weighting items. Weighting items can be used to reflect the relative importance of items within a domain—A higher score is given to a more “important” item.

WHEN TO ASSESS QoL

The QoL of an individual is changing continually; however, its measurement may be particularly appropriate at certain times or in specific circumstances. When choosing an instrument, the investigator must be confident that the measure is valid in that circumstance and that it probes issues relevant to the respondent. An isolated assessment is insufficient, particularly for children. The identification of the effects of therapy on QoL both in the short and long term may be of value. Assessment of QoL may be appropriate in particular circumstances. For example, at the beginning and end of therapy or at follow-up, when the acute impact of therapy has passed (e.g., 2–5 years following completion of therapy). Measurement of QoL may also be of value even if cure is not possible. For example, the QoL of the child may be the most important end point in the context of palliative care. Within clinical trials, when there is no difference in outcome for two or more different therapeutic options, treatment-specific QoL may be particularly important. Finally, in situations in which a treatment option may lead to only a small benefit in survival but may have a large, adverse impact on QoL, determination of QoL is essential. In cost-benefit analyses, QoL must also be considered.

CHOOSING A MEASURE OF QoL

As interest in measurement of QoL increases, the number of available measures will also expand. Several points should be considered when choosing a measure of QoL, particularly in the context of research. The use of a relatively brief questionnaire to assess the complex issue of QoL has limitations. The questionnaire must be sufficiently brief to be acceptable to, for example, a sick child or for use in large populations. However, there is clearly a compromise to be achieved between brevity and the need to assess comprehensively the several different attributes that influence QoL. The investigator must clearly define the issues to be measured and must consider the ability of the instrument to do so. The investigator must also be confident that adequate validity and reliability have been established for use with a particular cohort or must define ways in which this can be done in the course of the proposed investigation.

CONCLUSIONS

The long-established use of large, multicentre, randomised, controlled trials in paediatric oncology suggests that these trials are placed ideally to apply measures of QoL to the assessment of the impact of therapy on the life of the child or adolescent. It will be necessary to justify not assessing QoL in children when planning future studies, but the observer must be confident of the reliability and validity of any measure that is used.

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